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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,341	11/21/2000	Jennifa Gosling	19934-000711US	5168

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,341	GOSLING ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25, and 27-49* is/are pending in the application.

4a) Of the above claim(s) *1-24,28-36 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27,37-41 and 43-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-25 and 27-49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14, 17* .
4) ☒ Interview Summary (PTO-413) Paper No(s). 18 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 26 November 2002 (Paper No. 15) has been entered in full. Claims 25 and 27 are amended and claims 37-49 are added.

This application contains claims 1-24 and 28-36 drawn to an invention nonelected without traverse in Paper No. 11 (26 April 2001). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. It is noted that Applicant maintains a traversal of the restriction requirement between Groups VII and VIII. Applicant argues that claim 25 can encompass an additional formulation step as recited in claim 28 and that the Examiner will necessarily have to conduct a search of the method as recited in claim 28. Applicant's arguments are not found persuasive because the method of claim 25 is not a method of formulation. Claim 25 recites a method of identifying a modulator and is not a product claim. A non-coextensive search of the prior art would be required by the Examiner if the two groups were rejoined because searching the claimed steps of identifying a modulator will not necessarily find prior art on methods of formulating that modulator. A rejoinder of the two groups would also require the Examiner to make additional claim rejections. Furthermore, Applicant argues that in the restriction requirement issued in the parent of this application, the Examiner included claim 28 within the same restriction group as claim 25. It is noted that in the parent application (09/686,020), Applicant did not elect the group that included claims 25 and 28. However, had this group been elected, a second restriction would have been made to separate claim 28 from claim 25.

Newly submitted claim 42 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 42 is directed to formulating a modulator identified by the method as a pharmaceutical composition. As discussed above, this claim requires additional process steps and endpoints from the originally elected method of Group VII and searching all of the inventions in a single patent application would provide an undue search burden on the examiner because of the non-coextensive nature of these searches.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 42 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

It is noted to Applicant that the species requirement set forth in the Office Action of 25 March 2002 (Paper No. 8) is *withdrawn.* The chemokines recited in the claims are rejoined with the elected chemokine species of mMIP-1γ.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25, 27, 37-41, and 43-49 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 4 of the previous Office Action (Paper No. 11,14 August 2002) are *withdrawn* in view of the amended specification and title (Paper No. 15, 26 November 2002).

2. The objection to claim 25 regarding the recitation of non-elected species of chemokines is *withdrawn* in view of the rejoinder of the species by the Examiner.

3. The rejection of claims 25 and 27 under 35 U.S.C. § 112, first paragraph, as set forth at pg 5-7 of the previous Office Action (Paper No. 11, 26 November 2002) is *withdrawn* in view of Applicant's persuasive arguments and claim amendments (Paper No. 15, 26 November 2002). Please see section below on New 35 U.S.C. § 112, first paragraph rejections.

4. The rejections to claims 25 and 27 under 35 U.S.C. § 112, second paragraph, as set forth at pg 7-8 of the previous Office Action (Paper No. 11, 26 November 2002) are *withdrawn* in view of the amended claims (Paper No. 15, 26 November 2002).

5. The information disclosure statements filed on 23 July 2002 (Paper No. 17) and 26 November 2002 (Paper No. 14) have been considered. Several references have been crossed off the PTO-1449 forms because these references were considered and cited by the Examiner in an earlier Office Action (Paper No. 11, 14 August 2002).

Drawings

6. The formal drawings submitted 26 November 2002 (Paper No. 13) have been received. The drawings will be forwarded to the draftsperson for review at the time of allowance.

New Claim Rejections - 35 USC § 112

7. Claims 25, 27, 37-41, and 43-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the claims recite a method for identifying a modulator of the binding of CCX CKR polypeptide to a chemokine comprising (a) contacting an isolated or recombinant CCX CKR polypeptide having the amino acid sequence as set forth in SEQ ID NO: 2, or a

fragment or variant thereof, and the chemokine in the presence of a test compound and (b) comparing the level of binding of the chemokine and the polypeptide in (a) with the level of binding in the absence of the test compound wherein the CCX CKR polypeptide, fragment or variant can bind the chemokine in the absence of test compound, the chemokine is selected from the group consisting of ELC, SLC, TECK, BLC, CTACK, mMIP-1γ, and vMIPII, and a decrease in binding indicates that the test compound is an inhibitor of binding and an increase in binding indicates that the test compound is an enhancer of binding.

The specification teaches that the CCX CKR polypeptides "are variants and mutants characterized by conservative substitutions of amino acid residues of SEQ ID NO: 2" (pg 16, lines 24-27). The polypeptide may also be full-length or a fragment of the full-length protein. According to the specification, CCX CKR polypeptides may also be modified, relative to the amino acid sequence of SEQ ID NO: 2, in some manner, e.g. truncated, mutated, derivatized, or fused to other sequences...or contain insertions, deletion or substitutions of amino acid residues relative to SEQ ID NO: 2 (pg 16, lines 28-34; pg 17, line 1). However, the specification of the instant application does not teach variants of the polypeptide of SEQ ID NO: 2. The specification does not disclose methods or working examples to enable one skilled in the art to obtain amino acid substitution, deletion, or addition variants or any allelic variants from different species.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can

be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997,

Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that this issue could be overcome by removing the term "variant" from the claims.)

8. Claims 25, 27, 37-41, and 43-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite a method for identifying a modulator of the binding of CCX CKR polypeptide to a chemokine comprising (a) contacting an isolated or recombinant CCX CKR polypeptide having the amino acid sequence as set forth in SEQ ID NO: 2, or a fragment or variant thereof, and the chemokine in the presence of a test compound and (b) comparing the level of binding of the chemokine and the polypeptide in (a) with the level of binding in the absence of the test compound wherein the CCX CKR polypeptide, fragment or variant can bind

the chemokine in the absence of test compound, the chemokine is selected from the group consisting of ELC, SLC, TECK, BLC, CTACK, mMIP-1γ, and vMIPII, and a decrease in binding indicates that the test compound is an inhibitor of binding and an increase in binding indicates that the test compound is an enhancer of binding.

The specification teaches a human CCXCKR polynucleotide (SEQ ID NO: 1) and a polypeptide encoded by the nucleotide of SEQ ID NO: 1. However, the specification does not teach functional or structural characteristics of the CCX CKR polypeptide variants in the context of a cell or organism. The description of one CCX CKR polynucleotide species (SEQ ID NO: 1) and one polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants of the polypeptide of SEQ ID NO: 2.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of

isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated or recombinant CCX CKR polypeptide having the amino acid sequence of SEQ ID NO: 2, or a fragment thereof, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 25, 27, 37-41, and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Gunn et al. (U.S. Patent 6,110,695). It is noted that the Examiner has interpreted the polypeptide, Burkitt's Lymphoma Receptor-1 (BLR-1), as taught by Gunn et al., to be a structurally different *variant* of the CCX CKR polypeptide which is recited in the claims of the instant application.

Gunn et al. teaches a method identifying agents that modulate the interaction of BLC and a Burkitt's Lymphoma Receptor-1 (BLR-1). Gunn et al. discloses (a) contacting a cell expressing a BLR1 polypeptide with BLC and a candidate modulatory agent, and (b) detecting an activity, including binding of BLC to the BLR-1 polypeptide and comparing the activity detected in the presence of the candidate agent to a reference level, wherein an increase or decrease in said activity relative to said reference level indicates that the agent modulates the interaction of the BLC and BLR-1 polypeptides (col 5-6; claim 1). Gunn et al. also teaches that BLR-1 and BLC may be labeled wherein the label provides for direct detection as radioactivity, luminescence, fluorescence, optical or electron density, etc. or indirect detection such as an epitope tag, etc. (col 5, lines 43-53). Gunn et al. discloses that BLR-1 is expressed on the surface of a cell, which may reside in culture or in situ, ie, within the natural host (col 5, lines 61-65). (It is also noted that this issue could be overcome by removing the term "variant" from the claims.)

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
February 5, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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